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Research Article

Completion Thyroidectomy in Patients Diagnosed with Papillary Thyroid Cancer: Is There a Predictive Factor for Contralateral Lobe Tumor?

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Abstract

Objectives: Completion thyroidectomy (CT) is defined as the removal of residual thyroid tissue in a case of malignancy detected after a lobectomy for an indeterminate or non-diagnostic biopsy. Factors such as tumor diameter, aggressive histology, extrathyroidal spread, and positive surgical margin in papillary thyroid cancer (PTC) constitute CT indications. However, the type of surgery to be performed is controversial, especially in patients with a tumor diameter of 1 to 4 cm. Determination of predictive factors for a contralateral lobe tumor (CLT) in PTC would be helpful to avoid excessive treatment of patients with this common thyroid pathology.

The aim of this study was to determine any predictive factors and rate of detection of a CLT after CT in patients with PTC.

Methods: Medical records of patients who underwent a lobectomy with the final histological diagnosis of PTC between 2011 and 2016 were reviewed to obtain the following data: demographic data of the patients; tumor diameter, multicentricity, and subtype; extrathyroidal spread details; and vascular invasion rate. The patients were divided into 2 groups according to the results of the final histological examination after the CT: benign (Group 1) and malignant (Group 2).

Results: The data of 49 patients were retrospectively analyzed. A female to male ratio of 33/16 and a mean age of 47.59 years (23-77 years) were determined. Group 1 and Group 2 consisted, respectively, of 30 and 19 patients. No significant difference was found between the 2 groups regarding demographic data or tumor characteristics.

Conclusion: Our study did not determine a predictive factor for the presence of a CLT, and the rate of detection remains high. Additional, larger studies of the subject are necessary.

Keywords: Cancer; completion thyroidectomy; lobectomy; papillary thyroid carcinoma; pathology; predictive factor.

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Thyroid nodules are one of the most common endocrine pathologies in adult populations and can be diagnosed by physical examination (4-8%), ultrasonographic examination (10-41%) and autopsy (50%).[1] Though the majority of these nodules are benign, thyroid carcinoma is detected in about 5% of cases.[2, 3] Papillary thyroid cancer (PTC) is the most frequent histological subtype of thyroid cancer and the incidence of PTC increases over the years.[4] PTC usually has a slow course, rarely showing aggressive behavior. The cancer-specific mortality rate is less than 5% of patients with PTC, and most patients have an excellent prognosis.[5] Nonetheless, PTC should be evaluated carefully because of

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the potential for distant metastasis.

Removal of residual thyroid tissue in the case of malignancy detected after a lobectomy has practical benefits regarding patients' treatment.[6] Completion thyroidectomy (CT) is the conversion of the process to a total thyroidectomy (TT) with the removal of residual thyroid tissue after a subtotal thyroidectomy. A lobectomy may initially be preferred in order to avoid unnecessary thyroidectomies in patients with a fine needle aspiration biopsy (FNA) result that is suspiciously malignant or which is indeterminate.[5, 6]

Thyroid lobectomy is the recommended initial surgical approach in patients with findings of a solitary, cytologically indeterminate nodule; atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS); or a follicular neoplasm/suspicious for follicular neoplasm (FN/SFN), according to the 2015 guideline of the American Thyroid Association (ATA). However, this approach may be modified according to clinical or sonographic characteristics of the patient and patient preference, or molecular tests.[7] Suspicion of malignancy was reported as the reason for a recommendation of CT for patients with histology results of AUS/FLUS in 5% to 15% of cases, according to the Bethesda System for Reporting Thyroid Cytopathology.

CT for PTC decreases local recurrence, improves survival, and facilitates the follow-up.[8]

In the case of cancer detection after lobectomy, it is controversial to perform an intervention in the contralateral lobe.[6, 8] In patients with malignant histopathology, as of now, there is no accurate method or criterion to understand whether malignancy is present in the contralateral lobe. This study was designed to examine potential predictive factors and the rate of detection of a contralateral lobe tumor (CLT) after CT in patients with PTC detected after a lobectomy.

Methods

Medical records of patients who underwent a lobectomy for nodular goiter without a history of known malignancy and with a final histological diagnosis of PTC during the study period of 2011 to 2016 were reviewed to obtain the demographic data of the patients; the diameter, multicentricity, and subtype of the tumor; extrathyroidal spread details; and the vascular invasion rate. All of the patients were evaluated by a radiologist experienced in neck ultrasound (USG) in order to examine the remaining tissue and lymph nodes. This study was conducted in accordance with the 1964 Helsinki Declaration.

In our study, CT was performed on patients with extrathyroidal spread, a previous history of radiation to the neck, a tumor >4 cm in diameter, an aggressive variant of PTC, or the presence of multiple nodules or a nodule in the contralateral lobe. CT is performed for a tumor diameter <1 cm after lobectomy in cases of extrathyroidal spread or an aggressive variant of PTC. Patients with an aggressive variant of papillary cancer, tumor spread to the lateral compartment, or extrathyroidal spread for tumors >4 cm were treated with a central neck dissection, a lateral neck dissection, or both. After the lobectomy, 16 patients whose pathology result was the classic or follicular variant of PTC with a tumor <1 cm in diameter and without extrathyroidal spread, and whose follow-up USG had no pathological findings in the opposite lobe or the neck were followed up nonoperatively, according to the preference of the patient.

Patients under 18 years of age, cases of complementary thyroidectomy following bilateral subtotal thyroidectomy, and non-totalized complementary thyroidectomy were excluded. Informed consent was obtained from all of the patients.

The data were obtained through a review of the retrospectively maintained database. The patients were divided into 2 groups according to the final histological examination after the CT: benign (Group 1) and malignant (Group 2). Variables that could be predictive factors, such as age, tumor diameter, multicentricity, subtype, vascular invasion, and extrathyroidal spread were compared between these 2 groups.

All analyses were performed with the IBM SPSS Statistics for Windows, Version 21.0. software package (IBM Corp., Armonk, NY, USA) at the 95% confidence level and $p<0.05$ significance level. Quantitative variables were reported as the mean and SD; qualitative variables were described as numbers and percentages.

Results

In all, 40 of 217 patients who underwent lobectomy in this clinic had PTC, and 3 had medullary thyroid carcinoma. The incidence rate of cancer was 19.8% (n=43) in this series. The PTC incidence was detected as 18.4% (n=40). CT was performed for 37 of the 40 PTC patients. Twelve of the patients had a lobectomy at a different clinic and 37 had a lobectomy performed at our clinic; a total of 49 patients whose histopathological examination was reported as PTC after a lobectomy were enrolled in this study. The female to male ratio and the mean age were 33/16 and 47.59 years (23-77 years), respectively. The first surgical procedure was performed for benign indications (cosmesis, compression symptoms, >3.5 cm nodule) of nodular thyroid disease for 35 patients and AUS/FLUS or FN/SFN for 14 patients. The PTC subtypes were the follicular variant in 24 patients (48.9%), the classic variant in 24 patients (48.9%), and the tall cell variant in 1 patient (2%). The average time between

the 2 surgical procedures for patients included in the study was 93 days (54-130 days). In addition to CT, as a result of the patients' neck USG examinations and clinical evaluations, 2 of the patients had unilateral central neck dissection, and 1 had bilateral central and lateral neck dissection. The 2 patients who underwent a unilateral central neck dissection had 3 and 1 positive lymph nodes, respectively, and the patient who underwent a bilateral central and lateral neck dissection had 6 positive lymph nodes out of 22. While histopathological examination of the TT material revealed no malignancy in the contralateral lobe in 30 (61.2%) patients (Group 1), malignancy was determined in 19 (38.8%) patients (Group 2). The age of the patients, tumor subtype after the first operation, diameter, multicentricity of the tumor, extrathyroidal spread, and vascular invasion rates are provided in Table 1. A comparison of the age, subtype, diameter, multicentricity of the tumor, extrathyroidal spread, and vascular invasion rates is illustrated in Table 2. Micropapillary carcinoma was detected in 6 (31.5%) of the patients who had malignancy in the contralateral lobe.

Table 1. Demographic and histopathological features of patients after lobectomy (first operation)

	Mean±SD	Min-Max
Age (years)	47.0±13.3	23-77
Tumor diameter (cm)	2.17±1.27	0.2-5.5
	n	**%**
Vascular invasion		
No	39	79.6
Yes	10	20.4
Extrathyroidal spread		
No	43	87.7
Yes	6	12.3
Subtype		
Follicular variant	24	48.9
Classic variant	24	48.9
Tall cell variant	1	2.0
Contralateral lobe findings after CT		
Benign	30	61.2
Malignant	19	38.8

CT: Completion thyroidectomy.

Table 2. Comparison of demographic and histopathological features between groups

	Group 1 Mean±SD (Min-Max)		Group 2 Mean±SD (Min-Max)		p
Age (Years)	47.7±15.2 (23-77)		45.8±10.1 (31-63)		0.630
Tumor diameter (cm)	2.17±0.97 (0.2-4)		2.18±1.66 (0.4-5.5)		0.313
	n	**%**	**n**	**%**	
Age (Years)					
<45	15	50.0	8	42.1	0.590
>45	15	50.0	11	57.9	
Tumor diameter (cm) after first operation					
≤1	4	13.3	6	31.6	0.123
1-4	23	76.7	9	47.4	
≥4	3	10	4	21.1	
Multicentricity after first operation					
No	20	66.7	12	63.2	0.801
Yes	10	33.3	7	36.8	
Vascular invasion after first operation					
No	24	80.0	15	78.9	0.929
Yes	6	20.0	4	21.1	
Extrathyroidal spread after first operation					
No	27	90.0	16	84.2	0.547
Yes	3	10.0	3	15.8	
Subtype after first operation					
Follicular variant	16	53.3	8	42.1	0.442
Classic variant	14	46.7	10	52.6	
Tall cell variant	0	0.0	1	5.3	

There was no significant difference between the 2 groups regarding the mean age (p=0.590). While 7 of 19 (36.8%) patients who were diagnosed with malignancy had multicentricity, 10 of 30 (33.3%) patients without a malignant histopathology had multicentricity in the first operation.

Since the multicentricity rate was similar between groups, there was no significant difference to suggest it as a predictive factor (p=0.801). Furthermore, there was no significant difference in the comparison of the subtype and diameter of the tumor, extrathyroidal spread, or vascular invasion rates between groups as a predictive factor for a CLT (Table 2).

Discussion

Benign thyroidectomies are usually performed due to compression of the trachea or esophagus, cosmetic concern, or overt hyperthyroidism. Lobectomy is usually a satisfactory procedure for unilateral benign pathologies of the thyroid and when there is no pathology in the contralateral lobe in cases with AUS/FLUS and FN after FNA. Thyroid cancer has been reported as occurring in 3% to 16.6% of patients after thyroidectomy for benign diseases of the thyroid.[9, 10] Güner et al.[11] reported an incidence of 3.37% (n=9) for incidentally detected PTC among 314 patients operated for MNG.

In our study, the rate of thyroid cancer after a unilateral lobectomy was 19.8%. Indications for the first operation of all of the CT patients were a diagnosis of AUS/FLUS or SN/SFN after FNA in 14 patients, and lobectomy for benign indications of nodular goiter in 35 patients. Recently, it has been reported that incidentally detected PTC increased after thyroidectomy performed for benign thyroid pathologies. Lombardi et al.[12] indicated that 42% of the 933 cases of PTC identified in areas of endemic goiter were incidentally detected.[12] In our study, the incidence of incidental malignancy after unilateral thyroidectomy was 19.8% (n=43), and the PTC rate was determined to be 18.4% (n=40).

Histopathological evaluation of patients requiring a CT has revealed high rates of residual tumors.[13, 14] The residual tumor rate has been reported at 29% to 56.3%, in various studies.[14-17] Because detection of a multicentric tumor is thought to indicate an increased likelihood of a CLT, CT is recommended even when the tumor size is <1 cm.[17] High recurrence and residual tumor rates led surgeons to perform more CTs.

Histopathological examination of CT materials revealed malignancy in 19 patients (38.8%) in the contralateral lobe, in our study. Among 17 lobectomies with a multicentric tumor, the incidence of malignancy was 36.8%, which was similar to the rate of patients without a CLT (33.3%). Although multicentricity has been reported as a factor associated with the detection of CLT in the literature, in our study 20 (40.8%) of the patients with multicentricity detected in the previous operation did not have a CLT after CT. This requires detailed investigation of whether multicentricity alone is an indication for TT.

Thyroid malignancy consists of heterogeneous tumor groups with a broad spectrum of biological behavior. Appropriate treatment usually results in a high survival rate. There is a continuing debate about studies with large, randomized series and long-term follow-up comparing methods and treatment options for these tumors.[18, 19]

TT has been reported to reduce the local recurrence rate, improve survival, and facilitate follow-up in differentiated thyroid cancers, suggesting that inadequate tissue ablation is an independent factor that adversely affects prognosis.[8] The leading reasons for CT in our study were to optimize the radioiodine ablation of the remaining thyroid tissue and to ensure better postoperative follow-up, consequently contributing to recurrence and survival. Removal of the remaining thyroid tissue provides practical benefits regarding monitoring and treatment of patients with PTC.

Pacini et al.[20] found cancer in residual thyroid tissue in 80 (44%) of 182 patients who underwent CT with a diagnosis of PTC after lobectomy, and they also reported that they detected lymph node metastasis in 10 cases that did not have cancer in the remaining tissue. As a result of this research, if the diagnosis of PTC is made before surgery, TT should be performed, and if it occurs after a lobectomy, it should be completed to TT.

CT has not been adequately demonstrated to improve survival, but multifocal tumors are thought to necessitate CT.[21]

Multicentricity has been reported to be greater in the CTL in patients with multicentric papillary microcarcinomas.[17] Since multicentricity rates were similar in our groups, multicentricity was not helpful as a predictive factor to detect cancer in the remaining tissue.

Pellegriti et al.[22] examined 299 cases with PTC <1.5 cm in size and found that 30% of the patients had a multicentric tumor and lymph node metastases, 20% had extrathyroidal spread, and 3% had distant metastases. They reported that tumor aggressiveness increased as the tumor diameter increased.[22] In our study, we found that the tumor diameter was not a significant predictive factor in helping to determine the presence of a CLT.

When the histological subtypes of PTC were examined, the tall cell and diffuse sclerosing variants were more aggressive than the classic and follicular variants.[23] Follicular variant PTC tumors are typically smaller than classic variant PTC tumors and have a lower regional lymph node metastasis rate.[24, 25]

Ibrahim et al. [26] reported a rate of CLT of 48% after TT in a

study conducted on 97 patients. The presence of multicentricity and an aggressive subtype in the first operation was found to be more important than the initial tumor size in the decision to perform a CT.

The tissue remaining after a lobectomy is clinically relevant, as it may or may not be cancerous. Since this may lead to incomplete or excessive treatment and associated complications, the development of a predictive factor for these patients will be very valuable.

In the 2015 ATA guidelines there is no suggested predictive factor, but CT indications are presented for patients with cancer detected after a lobectomy; a tumor size >4 cm, extrathyroidal spread, or a worrisome histological variant.

All of the patients in our study were directed to the nuclear medicine clinic after undergoing a CT. In 3 patients who had high thyroglobulin levels during follow-up after radioactive iodine ablation therapy, distant metastases were detected with positron emission tomography–computed tomography, and these patients were once again treated with radioactive iodine ablation therapy. A patient with extrathyroidal spread >4 cm had a 1 cm LAP in the neck detected with USG performed after the detection of a high blood Tg level in postoperative follow-up. Excision was performed following a Tg washout result suggesting recurrence.

Conclusion

In our study, 79% of patients with tumors <1 cm in diameter and between 1 and 4 cm had a CLT. Our rate of CLT was high (38.8%). However, no significant predictive factor for CLT was found. Discussion of the limits of appropriate treatment and what constitutes over-treatment are still ongoing. We think that this is an issue that needs clarification in further investigation with larger series.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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